
Kruppel-like factor 4 (Klf4) prevents embryonic stem (ES) cell differentiation by regulating Nanog gene expression.

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Public Summary:

This study has elucidated the role of Klf4 in ES cell identity, reinforcing and aiding in the confirmation of its importance in the maintenance of pluripotency as well as selfrenewal. Klf4 may carry out this function by acting as a fast responding mediator to LIF-Stat3 signal changes, eventually affecting the expression of Nanog, which is well established as a key factor in maintenance of ES cell stemness.

Scientific Abstract:

Transcription factor Kruppel-like factor 4 (Klf4) is essential for somatic cell reprogramming. In addition, Klf4 seems to play a redundant role along with other Klf family proteins in embryonic stem (ES) cell self-renewal. However, how Klf4 regulates ES cell self-renewal and somatic cell reprogramming is still poorly understood. Here we report that Klf4 is required for both ES cell self-renewal and maintenance of pluripotency and that the expression of Klf4 prevents ES cell differentiation in response to withdrawal of leukemia inhibitory factor (LIF) or bone morphogenetic protein 4 (BMP4). In addition, Klf4 directly binds to the promoter region of Nanog and regulates its expression. Expression of Nanog prevents ES cell differentiation even when Klf4 gene expression is knocked down. On the other hand, knockdown of Nanog expression induces differentiation of ES cells that overexpress Klf4. Taken together, these results demonstrate that Klf4 functions upstream of Nanog in ES cell self-renewal and in preventing ES cell differentiation.

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